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Original Article

Solitary thyroid nodule: Diagnostic yield of combined diffusion weighted imaging and magnetic resonance spectroscopy

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ABSTRACT

Aim: The scope of this study is to evaluate the combined application of MR-DWI and MRS in differentiating between benign and malignant thyroid nodules.
Materials and methods: Total of 42 patients was enrolled in this study. DWI was done and ADC values were calculated. MRS was done and Choline peak as well as Cho/Cr ratio was evaluated.
Results: Patients were categorized into benign group (28 patients) (20 adenomatous nodules and 8 follicular adenomas) and malignant group (14 patients: 8 papillary carcinomas, 4 follicular carcinoma, 1 medullary carcinoma, and 1 anaplastic carcinoma).
The mean ADC values of benign nodules showed significantly high values than malignant ones (1.84 ± 0.36 versus $0.87 \pm 0.35 \times 10^{-3}$ mm^2/s respectively ($p < 0.0001$).
While no significant difference was detected among the ADC values of different benign lesions among different malignant pathological types.
By analyzing the ROC curve, the area under the curve (AUC) was (0.97) with ADC cutoff value of 1.5×10^{-3} mm^2/s was able in differentiating benign and malignant thyroid nodules with sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of 85.7, 89.2, 80.0, 92.5% respectively while KAPPA test = 0.73 and $p < 0.0001$.
All malignant thyroid nodules had a significant choline peak (n = 14, 100%) at MR spectroscopy (Figs. 2 and 3) while benign nodes showed choline peak in only two cases (n = 3, 10.7%).
The mean Cho/Cr ratio showed significant higher values in malignant thyroid nodules compared to the benign ones (3.1 ± 0.85 versus 1.09 ± 0.13) ($p = 0.001$).
While no detected significant difference of Cho/Cr ratio among different types of malignancy (2.86 ± 0.66, 2.95 ± 0.90, 4.21 and 4.53 for papillary carcinomas, follicular carcinoma, medullary carcinoma, and anaplastic carcinoma respectively, $p = 0.85$).
The MRS sensitivity, specificity PPV and NPV in differentiating between benign and malignant thyroid nodules were as following 100, 89.3, 82.4 and 100% respectively while Kappa test was 0.84 and $p < 0.0001$. Combination of both DWI and MRS showed higher diagnostic values than each of DWI and MRS alone with sensitivity, specificity, PPV and NPV of 100, 96, 93.3 and 100% respectively while Kappa test was 0.94 of and p value <0.0001.
Conclusion: Combination of DWI and MRS techniques can help in the differentiation between benign and malignant solitary thyroid nodules.
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1. Introduction

Thyroid nodules are common finding in about 4–7% of general population that makes it the commonest problem observed by endocrine surgeons. Most of the solitary thyroid nodules are benign while malignant ones represent nearly 5% of solitary thyroid nodules so it is a challenge to differentiate benign from malignant thyroid nodules. While fine-needle aspiration cytology (FNAC) has an accuracy of up to 97% in expert hands, it is limited by pain, hematoma formation risk, and inaccurate differentiation between benign and malignant follicular nodules [1,2].

The need to reduce the unnecessary surgery and financial cost supports the importance of application of pre-surgical non-invasive imaging modalities [3].

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While ultrasound is widely used in thyroid lesions imaging, there is no solitary reliable ultrasound criterion to discriminate between benign and malignant thyroid nodules accurately with extremely variability of its specificities, sensitivities, NPV and PPV among different studies, and no specific feature that has combined high sensitivity and high PPV for cancer thyroid [4–6].

Conventional MRI sequences are not able to rule out malignant thyroid nodules or assess the metabolic changes of thyroid nodules so there is a need for using of more advanced techniques [7–11].

Proton (1H) MR spectroscopy (1H MRS) is a non-invasive technique which can evaluate the cell metabolite and chemical changes and it was shown as a promising technique in the assessment of malignancy with multiple reports that supported its validity. In MRS suppression of water and lipid resonances at 4.7 and 1.3 ppm (ppm) respectively is needed, also the magnetic field should be as homogeneous as possible by shimming. Horizontal axis of MRS corresponds to the metabolite resonance frequency in respect to the water resonance peak. While the vertical axis shows the relative amplitude of metabolite signal in arbitrary units. MRS shows quantitative data (metabolite presence or absence) and semi-quantitative (metabolites amplitude and its relative ratio to control) [12–18].

Additionally, diffusion-weighed MRI (DW-MRI) is a non-invasive technique that can monitor the diffusion of water proton intra-, extra- cellular as well as through cell membrane. DWI-MRI depends on the Brownian water protons motion. Applying of magnetic field gradient dephases the water molecules while applying of a second opposing gradient rephrases it. Movement of the water molecules between these two opposing gradients will result in signal loss. As this motion is hampered by fibers and intracellular organelles, the microstructure and physiological tissue state affect the DW-MRI. These signal changes can be quantified and reflected by apparent diffusion coefficient (ADC) [19–25].

The scope of the current study is to assess the combined application of the DWI and MRS in differentiation between benign and malignant thyroid nodules.

2. Materials and methods

2.1. Patients

This prospective study comprised of 49 patients with solitary thyroid nodule who are ongoing to be subjected to histopathological examination either by surgery or FNAB. MRI examination including DWI and MRS was done 2–7 days prior to FNAB or surgery. Seven patients were then excluded because of poor image quality and artifact (two on MRS and two on DWI) while three patients had FNAB failure with indeterminate diagnosis. So finally total of 42 patients (27 female and 15 males) were enrolled in this study. The age range was (21–65 years) with mean age of 45.4 years). Approval from institutional review board as well as informed patient consent was achieved.

2.2. MR imaging protocol

2.2.1. Conventional MRI

MR examination was done using a 1.5-T MR (Achieva, Philips Medical Systems, Netherland B.V.). Patients were positioned in supine with application of neck circular polarization surface coil and centralization of the thyroid in the field of view. Patients were instructed to avoid movement and swallowing during the image acquisition. Localizer was taken in axial, sagittal and coronal planes, the conventional MRI in axial, coronal as well as sagittal planes was done by T1 and T2 weighted images. The parameters used were: repetition time (TR)/echo time (TE) ms: 450–650/8–9 for T1-weighted images and 3000/100 for T2-weighted fast spin echo, slice thickness/gap of 2–4 mm and 1 mm and field of view (FOV) of 210–250 mm while the flip angle was 90 degree.

2.2.2. Diffusion-weighted images

Axial plane was used using the sequence of single shot echo planar imaging (EPI) sequence. The parameters used were TR/TE 2000–2600 ms/65–70 ms, with a slice thickness of 3–4 mm and slice interval of 1 mm, intersection gap, FOV 210–250 mm. b values used were 0 and 500 s/mm^2. The scan time lasts 35 s. in average.

2.2.3. 1-H magnetic resonance spectroscopy (MRS)

Automatic shimming was applied to ensure homogeneity of the magnetic field while manual shimming with linewidth of 12–14 Hz. was used in case of difficult automatic shimming due to significant susceptibility differences.

Point resolved spectroscopic sequence (PRESS) – using single voxel technique with the parameters of; TR/TE = 2000/135 ms, spectral bandwidth 1000 Hz, signal acquisition 64, and number of points 512. Chemical shift-selective suppression was applied for water suppression. The data was automatically processed (average scan time was 4:35 min).

The volume of interest (VOI) was carefully positioned on the thyroid nodule in axial, coronal and sagittal planes to limit inclusion of surrounding normal tissue.

Spectra were analyzed for the occurrence of choline (Cho) and Creatine (Cr) peak at 3.22 and 3.03 ppm respectively, automatic calculation of Cho/Cr ratio was achieved then.

2.2.4. Calculation of the ADC value

Incorporated software in same sequence of diffusion weighted image could automatically calculate ADC map. A region of interest (ROI) was applied electronically applied on the ADC map by tracing around the solid thyroid nodule and around solid part of mixed cystic and solid nodule.

2.3. Statistical analysis

According to the histopathological results of thyroid nodules, the patients in the current study were classified into benign and malignant groups. Statistical Package for the Social Sciences for Windows (SPSS) software version 17 was used for analysis. The mean and standard deviations value of ADC and Cho/Cr ratio were calculated for the groups.

One way analysis of variance (ANOVA) and T-test were applied to analyze the difference in ADC and Cho/Cr ratio among the variable histopathological thyroid nodules types.

Application of receiver operating characteristic (ROC) curve was done to evaluate the diagnostic power of the ADC value. Multiple ADC thresholds values were analyzed to find out the best cutoff value estimated by Kappa test in differentiation between benign from malignant nodules.

Calculation of the sensitivity, specificity, positive predictive value (PPV) negative predictive value (NPV) and Kappa test of DWI, MRS and combined both techniques to differentiate between benign and malignant thyroid nodules was done.

The probability (p value) of <0.05 was considered significant.

3. Results

49 patients with solitary thyroid nodule were subjected to DWI and MRS before the pathological examination. Seven patients were then excluded from the study due to poor quality of images (n = 4) and FNAB indeterminate diagnosis (n = 3). So finally we had total of 42 patients completed this study.

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